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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER

PRIEBE, SCOTT DAVID

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 07/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/843,598

Applicant(s)

HORVITZ ET AL.

Examiner

Scott D. Priebe

Art Unit

1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 30 June 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 30 June 2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 1-5 and 7-11.

Claim(s) objected to: _____.

Claim(s) rejected: 12-16 and 18-22.

Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☐ Other: _____.

Scott D. Priebe

Scott D. Priebe
Primary Examiner
Art Unit: 1632

Continuation of 3. Applicant's reply has overcome the following rejection(s): the rejections of claims 1-22 and 1-11 (new matter) for failing to comply with the written description requirement; the rejection of claims 1-11 for failing to comply with the enablement requirement; and the rejection of claims 1-11 under 112, 2nd para.

Continuation of 5. does NOT place the application in condition for allowance because: Only the rejection of claims 12-16 and 18-22 for lack of enablement remains. The amendment overcomes those grounds of rejection pertaining to the scope of the nematode used in the assay. The only remaining issue is whether the claimed method is enabled for identifying a test compound that modulates uptake of serotonin by a SERT due to modulation of the activity of a second target. Most of the claims are not limited to any particular compounds, e.g. those known to modulate uptake of serotonin by a SERT, nor are most limited to any specific "defined behavior", e.g. a behavior characteristic of the CeSERT mutant.

Appellant argues that reversal of a mutant behavioral phenotype by the test compound would indicate that the compound is modulating serotonin reuptake by a SERT-independent pathway. However, this ignores the more likely alternative explanation that the compound is acting on a pathway that is independent of serotonin altogether and the behavior has nothing to do with serotonin metabolism or utilization. The method as claimed does not allow one to distinguish between these possibilities. Furthermore, the claims are not limited to identifying a compound based on its ability to reverse the mutant behavioral phenotype, the defined behavior could be anything including behaviors that have not been correlated to, or have nothing to do with, changes in serotonin reuptake or serotonin activity, e.g. the nematode moves in circles or moves away from food, rather than toward it, in the presence of the compound. To illustrate, one can predict with certainty that the nematode would display a different behavior if treated with cyanide, a neurotoxin, a chemo-attractant, a laxative, or an anesthetic, but one would not conclude from such a behavioral change that serotonin uptake was involved, and even if it was, the method as recited would not reveal that connection between the behavior and serotonin. There are likely to be far more compounds that would cause a change in behavior of the mutant nematode by mechanisms unrelated to serotonin than due to modulation of serotonin uptake, and the method as recited does not allow one to distinguish between the possibilities. One would know no more about whether the compound affected the serotonin pathway after performing the method than was known before performing the method.

Also, the method of claim 1 is directed to determining whether a compound known to affect serotonin reuptake has any side-effects, i.e. interacts with a second target in a serotonin-independent pathway (page 12 of reply). If such a compound, e.g. a serotonin reuptake inhibitor, is used in the method of claim 12, the method steps would be the same. Yet Appellant is arguing that the same result that indicates that the serotonin reuptake inhibitor has a serotonin-independent side-effect with the method of claim 1, also indicates that the compound is acting on a second target to modulate serotonin reuptake by a SERT with the method of claim 12. These two conclusions are mutually exclusive. The conclusion reached as in claim 1 makes sense, i.e. since the SERT is absent, the behavioral change is probably not due to serotonin uptake.

In addition, the specification discloses that MOD-5 is likely to be the only SERT in *C. elegans*. First, the three specific *C. elegans* used in the assay have either reduced or no CeSERT function. Thus, any change in behavior is unlikely to be mediated by a SERT. Consequently, it is unclear how a change in behavior of the the nematode induced by a test compound could be correlated at all "modulating the uptake of serotonin by a serotonin reuptake transporter" as recited in the preamble. Rather, one would conclude that however the compound is acting, it is not modulating serotonin uptake by a SERT, and would not modulate serotonin uptake by a SERT, since SERT activity was not required, i.e. the compound acts by a SERT-independent method that may or may not have anything whatsoever to do with serotonin or the remaining components of the serotonin pathway in the mutant nematode. There is no correlation or nexus between the goal of the method as set forth in the preamble, and the recited method steps.